


# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference C163517PC ADI/jhl		<b>FOR FURTHER ACTION</b>		See Form PCT/PEA416
International application No. PCT/EP2004/013907		International filing date (day/month/year) 07.12.2004		Priority date (day/month/year) 29.12.2003
International Patent Classification (IPC) or national classification and IPC INV. A61K38/20 A61K7/06 A01K67/027 A61P17/14				
Applicant UNIVERSITÄTSKLINIKUM MÜNSTER et al.				
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 9 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input checked="" type="checkbox"/> sent to the applicant and to the International Bureau a total of 6 sheets, as follows:</p> <p><input checked="" type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>				
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the report</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input checked="" type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p>				
Date of submission of the demand  07.01.2005		Date of completion of this report  28.03.2006		
Name and mailing address of the international preliminary examining authority:  European Patent Office - Gitschiner Str. 103 D-10958 Berlin Tel. +49 30 25901 - 0 Fax: +49 30 25901 - 840		Authorized officer  Ceder, O  Telephone No. +49 30 25901-342		



INTERNATIONAL PRELIMINARY REPORT  
ON PATENTABILITY**Box No. I Basis of the report**

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language, which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
  - ☐ publication of the international application (under Rule 12.4)
  - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements\*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

**Description, Pages**

1, 2, 5-29 as originally filed

3, 4 received on 02.09.2005 with letter of 01.09.2005

**Sequence listings part of the description, Pages**

1-5 as originally filed

**Claims, Numbers**

1-23 received on 02.09.2005 with letter of 01.09.2005

**Drawings, Sheets**

1/5-4/5 as originally filed

5/5 received on 02.09.2005 with letter of 01.09.2005

☒ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
  - ☐ the claims, Nos.
  - ☐ the drawings, sheets/figs
  - ☐ the sequence listing (*specify*):
  - ☐ any table(s) related to sequence listing (*specify*):
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages
  - ☐ the claims, Nos.
  - ☐ the drawings, sheets/figs
  - ☐ the sequence listing (*specify*):
  - ☐ any table(s) related to sequence listing (*specify*):

\* If item 4 applies, some or all of these sheets may be marked "superseded."

**INTERNATIONAL PRELIMINARY REPORT  
ON PATENTABILITY**

International application No.  
PCT/EP2004/013907

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**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

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1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 15 and 23 with respect to industrial applicability

because:

☒ the said international application, or the said claims Nos. 15 and 23 with respect to industrial applicability relate to the following subject matter which does not require an international preliminary examination (specify):

**see separate sheet**

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

☐ has not been furnished

☐ does not comply with the standard

the computer readable form

☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

**INTERNATIONAL PRELIMINARY REPORT  
ON PATENTABILITY**

International application No.  
PCT/EP2004/013907

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**Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

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1. Statement

Novelty (N)	Yes: Claims	3, 4, 8-22
	No: Claims	1, 2, 5-7, 23
Inventive step (IS)	Yes: Claims	
	No: Claims	1-23
Industrial applicability (IA)	Yes: Claims	1-14, 16-22
	No: Claims	

2. Citations and explanations (Rule 70.7):

**see separate sheet**

**INTERNATIONAL PRELIMINARY REPORT  
ON PATENTABILITY**

International application No.  
PCT/EP2004/013907

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**Supplemental Box relating to Sequence Listing**

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**Continuation of Box I, item 2:**

1. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this report has been established on the basis of:
  - a. type of material:
    - ☒ a sequence listing
    - ☐ table(s) related to the sequence listing
  - b. format of material:
    - ☒ in written format
    - ☒ in computer readable form
  - c. time of filing/furnishing:
    - ☒ contained in the international application as filed
    - ☒ filed together with the international application in computer readable form
    - ☐ furnished subsequently to this Authority for the purposes of search and/or examination
    - ☐ received by this Authority as an amendment on
2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional observations, if necessary:

**INTERNATIONAL PRELIMINARY  
REPORT ON PATENTABILITY  
(SEPARATE SHEET)**

International application No.

PCT/EP2004/013907

**Re Item III**

Non-establishment of opinion with regard to industrial applicability

Claims 15 and 23 relate, at least partly, to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

**Re Item V**

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

**1. Documents**

1.1 Reference is made to the following documents:

- 1.2 **D1:** Lindner et al., J. Invest. Dermatol., vol. 110, 1998, pp. 457-458  
**D2:** US2003/0114526

**2. Novelty (Art. 33(2) PCT)**

- 2.1 The present application does not satisfy the criterion set forth in Article 33(2) PCT because **the subject-matter of claims 1, 2, 5-7 and 23 is not new** in respect of prior art as defined in the regulations (Rule 64(1)-(3) PCT).
- 2.2 The present application is concerned with the use of IL-15 polynucleotides, polypeptides and/or agonists for the stimulation of hair growth.
- 2.3 Document **D1** discloses (page 457, right-hand column, fourth paragraph; page 458, left-hand column) the inhibitory effect of IL-15 on keratinocyte apoptosis in hair bulbs. The

inhibition of apoptosis of the hair bulbs must at least implicitly be considered as stimulation of hair growth. **D1** further suggests the use of IL-15 receptor agonists in chemotherapy-induced alopecia.

2.4 Document **D1**, thus, explicitly or implicitly, destroys the novelty of claims 1, 2, 5-7 and 23.

2.5 Claims 3, 4, and 8-22 contains subject-matter that is novel over the cited prior art.

### 3. Inventive step (Art. 33(3) PCT)

3.1 The present application does not satisfy the criterion set forth in Article 33(3) PCT, because **the subject-matter of claims 1-23 does not involve an inventive step** (Rule 65(1)(2) PCT).

3.2 Even if claim 1 could be considered novel, it can not be considered inventive over **D1**. Document **D1** discloses the use of IL-15 to inhibit apoptosis in hair bulbs in vivo (page 457, right-hand column, fourth paragraph; page 458, left-hand column) and suggests its relevance in alopecia. A decreased apoptosis (death of cells) must be considered positive for the possibility of the hair bulbs to continue to produce hair. A dead cell does not produce any hair. The person skilled in the art, trying to find a method to increase the production/growth of hair would, thus, have the incentive to try and use IL-15 to decrease the death of cells and increase the potential of hair growth. In doing so he would arrive at the subject-matter of claim 1. No inventive activity can thus be acknowledged for claim 1 or 2.

3.3 Claim 3 is concerned with the use of IL-15 polynucleotides, polypeptides and/or agonists for the stimulation of hair growth, together with a second hair growth stimulating compound.

3.4 The subject-matter of claim 3, differs from that of **D1**, in that it concerns the use of a second active compound together with IL-15.

- 3.5 This difference can, however, not be considered as involving an inventive step (Article 33(3) PCT). The use of additional active compounds in compositions for affecting hair growth is already known, e.g. from **D2** (claim 8). It would be obvious for a person skilled in the art to combine the teachings of **D1** with the additional compounds of **D2** to arrive to the subject-matter of present claims 3 and 4. No inventive activity can, therefore, be acknowledged for claims 3 and 4.
- 3.6 None of claims 5-13 seem to contain any subject-matter which together with the subject-matter with any of the claims they depend upon could form the basis for an inventive activity.
- 3.7 Claim 14 is concerned with a transgenic animal expressing the state of the art IL-15 polynucleotide of claim 1. To obtain a transgenic animal expressing a known nucleic acid can not be considered inventive, but is only the mere application of state of the art technology, known to any person skilled in the art. Claim 14 is, thus not inventive.
- 3.7 Claims 15 and 16 are concerned with methods for stimulating hair growth in an animal by transforming the animal with the state of the art IL-15 polynucleotide of claim 1 or treating the animal with the composition of claim 1. In view of **D1** this can not be considered inventive.
- 3.8 None of claims 17-23 seem to contain any subject-matter that, in combination with the subject-matter of any of the claims they depend on, can be considered inventive.

#### **4. Further comments for a national/regional phase**

- 4.1 For the assessment of the present claims 15 and 23 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.



**INTERNATIONAL PRELIMINARY  
REPORT ON PATENTABILITY  
(SEPARATE SHEET)**

International application No.

PCT/EP2004/013907

- 4.2 The Applicant has, in his letter of 01.09.2005, argued that **D1** merely discloses the effect of IL-15 on apoptosis and speculates on its potential use in alopecia treatment and that the application shows (page 10, lines 17-20) that "IL-15 will not merely prevent apoptosis but also stimulate and promote growth of the cells". This might be true, but the discovery of a mode of action of a known or obvious use does not make the use novel or inventive, per se.
- 4.3 For the EPO, claim 1 can not be considered as a proper "second medical use claim". Such a claim must include the disease that should be treated. "Stimulating hair growth" is not a disease but rather a mode of action, which is not allowable in a "second medical use claim". Redrafting the claim in the proper format and including the disease (e.g. alopecia) would, however, not make the claim inventive over **D1**.